REMARKS

Claims 1-7, 9, 11-22, 24, 26, and 28-33 were finally rejected on June 3, 2004. Claims 31 and 32 have been cancelled herein without prejudice. Thus, claims 1-7, 9, 11-22, 24, 26, 28-30, and 33 are pending.

On September 3, 2004, Applicants appealed the Examiner's rejections and filed an Appeal Brief. An Examiner's Answer was mailed December 3, 2004, in response to Applicants' Appeal Brief. The following remarks are in response to the Examiner's Answer.

In light of these amendments and the following, Applicants respectfully request reconsideration and allowance of claims 1-7, 9, 11-22, 24, 26, 28-30, and 33.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 31 and 32 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully disagrees. To further patent prosecution; however, claims 31 and 32 have been cancelled herein without prejudice. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected all the claims as being obvious presenting five separate rejections under 35 U.S.C. § 103(a), each of which has been presented previously in the record. From statements throughout the Examiner's Answer, it appears the Examiner believes that it would have been obvious to use an attenuated measles virus as a convenient vector to deliver measles virus nucleic acid. For example, on page 8, the Examiner stated that "it would have been obvious to one of ordinary skill in the art to use the attenuated measles virus taught by Weibel as a convenient vector for the measles virus DNA." On page 9, the Examiner stated that:

> one of ordinary skill in the art would have had further grounds for believing that the use of an attenuated measles virus as a vector would have no effect on the operability of the measles virus DNA to destroy cancer cells. As both the whole virus and the isolated DNA have been shown to reduce tumors, there would be no reason for one of ordinary skill in the art to expect anything but success in the use of an attenuated virus as a vector for the DNA.

Applicants respectfully disagree. At the time Applicants filed, a person have ordinary skill in the art would have known that attenuated measles viruses are not interchangeable with wild-type whole measles viruses or isolated plasmid DNA as the Examiner appears to contend. According to the Takeda *et al.* reference (*J. Virol.*, 72:8690-8696 (1998)), measles virus attenuation is associated with impaired gene transcription. For the Examiner's convenience, a copy of the Takeda *et al.* reference is provided with the accompanying Information Disclosure Statement. Briefly, the Takeda *et al.* reference discloses comparing fresh infectious measles virus isolates and attenuated versions of those isolates (*e.g.*, the 9301B-9301V measles virus pair). The authors compared the entire genome sequences, the functions of envelope glycoproteins (F and H proteins), and gene expression and replication. As stated on page 8692, the "9301B virus [pathogenic virus] caused severe CPE [cytopathic effects], indicated by extensive cell fusion (giant-cell formation), whereas no such strong CPE was found for the 9301V virus [attenuated virus]." In addition, the pathogenic 9301B virus caused extensive pathogenicity in monkeys, while the attenuated 9301V virus did not. *See*, Table 1 on page 8692.

According to the authors, these differences between the pathogenic and attenuated measles viruses are not attributed to a functional impairment of the F or H glycoproteins, but rather are attributed to impaired gene transcription. In fact, on page 8694, the authors state that:

> the gene transcription of 9301V virus in B95a cells was significantly impaired compared with that of the 9301B virus. This resulted in reduced levels of the gene products, including the F and H proteins, which in turn could clearly explain the reduced level of 9301V induced fusion in B95a cells.

A person having ordinary skill in the art reading the Takeda *et al.* reference would have appreciated that the reported findings appear to be generally applicable to measles virus attenuation given that studies with two additional pairs of wild-type and Vero cell-adapted strains yielded "very similar patterns of transcriptional attenuation." *See*, page 8693.

Applicants respectfully submit that a person having ordinary skill in the art reading the combination of cited references together with the Takeda *et al.* reference would not have been motivated to administer an attenuated measles virus to a mammal to reduce the number of viable

cancer cells in that mammal. Thus, the combination of cited references does not render the presently claimed invention obvious.

In light of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

CONCLUSION

Applicants submit that claims 1-7, 9, 11-22, 24, 26, 28-30, and 33 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned attorney at the telephone number below if such will advance prosecution of this application. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

Date: April 27, 2005

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